

APPLICANT(S): LEVY, Andrew  
SERIAL NO.: 10/748,177  
FILED: December 31, 2003  
Page - 4 -

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#### REMARKS

The present response is intended to be fully responsive to all points of objection and rejection raised by the Examiner and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

A telephonic interview with the Examiner was conducted on February 16, 2007, in which Applicant presented the basis for support for the claims as previously amended. Specifically, Applicant pointed out that by amending "vascular" to "cardiovascular" in the independent claims, and removing stroke from the claims dependent thereon, the claims were focused on complications related to the heart. Furthermore, Applicant pointed out additional support for the benefit of antioxidant therapy when diabetes is combined with a haptoglobin 2 phenotype, in a recent publication (Blum et al., Haptoglobin genotype determines myocardial infarct size in diabetic mice, Journal of the American College of Cardiology 2007;49:82-87 ["Blum"]); attached herein and included in an IDS attached herewith).

During the discussion, the Examiner was not clear that the limitation to cardiovascular excluded stroke, nor of the persuasiveness of the Blum paper (discussed without being seen) in light of the data in Tables 5 and 6. These concerns are addressed in the remarks further below.

#### Response to IDS filed 3/24/06

The Examiner pointed out that although an IDS had been filed containing the references cited on pages 48-54 of the specification, the statement that these were cited by a foreign patent office within 3 months must have been erroneous since these references were cited in the specification as filed. Applicant regrets the oversight and encloses herewith a new IDS Form with the correct attribution of the references. Consideration of the references is now respectfully requested.

#### Status of the Claims

Claims 1, 3, 12-15, 17, and 26-28 are pending in the application.

APPLICANT(S): LEVY, Andrew  
SERIAL NO.: 10/748,177  
FILED: December 31, 2003  
Page - 5 -

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**CLAIM REJECTIONS: 35 U.S.C. § 112 - ENABLEMENT**

The Examiner rejected claims 1, 3, 12-15, 17 and 26-28 under 35 U.S.C. § 112, first paragraph. The Examiner contends that while the specification is enabling for a method for determining a potential of a diabetic patient to benefit from vitamin E therapy for treatment of CV death or MI wherein the benefit from said vitamin E therapy to a patient having a haptoglobin 2-2 phenotype is greater compared to patients having haptoglobin 1-2 phenotype or 1-1 phenotype, it does not reasonably provide enablement for any antioxidant therapy for treatment of any cardiovascular complication. The Examiner asserts the art is unpredictable for reasons of, for example, the lack of effect of vitamin treatment on LDL levels in diabetic patients in Levy et al., Diabetes Care, vol. 27, No. 4, pages 925-930, April, 2004, the irreproducibility of correlations of genetic variations, associations, and drug susceptibility in the art, and lack of correlation with stroke. The Examiner goes on to point out that a large quantity of experimentation would be required to establish associations and support the claims as broadly defined and correlated with, for example, diabetic retinopathy, nephropathy or neuropathy.

Applicant respectfully requests reconsideration of the rejection in light of amendments made previously to the claims.

With regard to the scope of complications in the claims as last amended, cardiovascular complication are intended to refer to complications involving the heart, and exclude stroke as well as diabetic retinopathy, nephropathy or neuropathy. Applicants point out the correlation between vitamin E and CV death and MI in Table 5, and between ramipril and the composite endpoint that includes cardiovascular endpoints, in Table 4

Moreover, further support for the breadth of the claims is provided by the Blum article. Blum showed that diabetic mice carrying the haptoglobin 2 variant were more susceptible to myocardial ischemia/reperfusion injury as well as being significantly benefited by antioxidant treatment (in this case, the antioxidant BXT-51072). While the studies were not conducted in humans, the data fully supports the findings in the instant specification regarding benefit of antioxidant treatment for cardiovascular complications.

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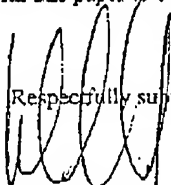
APPLICANT(S): LEVY, Andrew  
SERIAL NO.: 10/748,177  
FILED: December 31, 2003  
Page - 6 -

## CONCLUSION

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned.

Please charge any fees associated with this paper to deposit account No. 50-3355.



Respectfully submitted,

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Dated: May 7, 2007

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